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PATENT
Attorney Docket No.: DART1110-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Craig et al.	Art Unit:	1642
Serial No.:	09/483,184	Examiner	K. Canella
Filed:	January 14, 2000		
Title:	Mcl-1 GENE REGULATORY ELEMENTS AND A PRO-APOPTOTIC Mc1-1 VARIANT		

Box NON-FEE AMENDMENT
Commissioner for Patents
Washington, D.C. 20231

AMENDMENT IN RESPONSE TO THE OFFICE ACTION

Responsive to the Office Action mailed July 3, 2001 (Paper No. 9), entry of the amendments and reconsideration of the application in view of the amendments and the following remarks respectfully are requested.

I. AMENDMENTS

Please cancel claims 22 to 81 without prejudice.

II. REMARKS

Upon entry of the amendment, claims 1 to 21 will be pending.

CERTIFICATION UNDER 37 CFR §1.8
I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service as first class mail on this date, October 2, 2001, in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231.
Aldon Griffis *(Name of Person Mailing Paper)*
Aldon Griffis *(Signature)* October 2, 2001 *(Date)*

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A. Regarding the Amendment

Pursuant to the restriction requirement, claims 22 to 81 are cancelled herein without disclaimer, and without prejudice to Applicants pursuing subject matter encompassed within one or more of the claims in an application claiming the benefit of priority of the subject application.

B. Rejection under 35 U.S.C. § 101

The rejection of claims 1 to 21 under 35 U.S.C. § 101 as allegedly lacking utility is respectfully traversed.

It is acknowledged in the Office Action that it is known in the art that recombinant overexpression of the Mcl-1 protein can enhance survival of various cells placed under apoptosis-inducing conditions *in vitro* and in transgenic animals (citing to Townsend et al., and Zhou et al.). It is alleged, however that present specification does not demonstrate the use of the claimed gene regulatory region in the control of apoptosis.

The claims are directed to compositions of matter, including, for example, claims 1 to 9, which are directed to an Mcl-1 gene regulatory element. The specification discloses an Mcl-1 gene regulatory element, which comprises nucleotide sequences upstream of the Mcl-1 coding sequence (see, for example, Figure 3). The specification also discloses that the Mcl-1 gene regulatory element, when linked to a reporter gene, regulates expression of the reporter gene in a manner similar to that reported for regulation of expression of Mcl-1 in intact cells (see, for example, page 65, line 21, to page 66, line 14; and page 72, line 30, to page 74, line 20).

It is submitted that there is no requirement that the claimed regulatory element have a demonstrated use in the "control of apoptosis"; any patentable utility is sufficient to meet the utility requirement where the claim does not recite a particular utility (see, for example, Cross v. Iizuka 224 U.S.P.Q.739, 743 (Fed. Cir. 1985)). In the present case, the specification discloses, for example, that the claimed regulatory element regulates expression of Mcl-1 polypeptide, including an Mcl-1 variant polypeptide (see below; see, also, Example 1 of the

specification), and further discloses patentable utilities for the claimed gene regulatory element. For example, the specification discloses that an Mcl-1 gene regulatory element of the invention can be used, for example, as a tool for identifying an agent that can modulate expression of a nucleotide sequence operatively linked to the regulatory element (page 47, lines 1-17). In addition, the specification discloses that a regulatory element of the invention can be linked to a heterologous nucleic acid molecule, for example, for the purpose of co-expressing the heterologous nucleic acid molecule in a cell with endogenous Mcl-1 (page 46, lines 18-26).

Applicants submit that such utilities as disclosed in the specification are "well known" utilities because it is routine in the art to use a newly isolated gene regulatory element as a tool to identify agents that regulate expression from the element, or to co-express a reporter or other molecule in a cell with the polypeptide normally expressed from the regulatory element. Furthermore, it is submitted that the disclosed utilities are "specific" because only an Mcl-1 gene regulatory element can be used for the disclosed purposes; "substantial" because Mcl-1 gene expression is known to be associated with apoptosis and, therefore, the Mcl-1 gene regulatory element provides a tool that allows one skilled in the art to identify cells in which Mcl-1 has been induced; and "credible" because such uses and methods as disclosed for the Mcl-1 gene regulatory element of the invention similarly have been practiced with other gene regulatory elements.

It is further acknowledged in the Office Action that Yang et al. teach increased Mcl-1 mRNA expression is leukemia cells exposed to phorbol esters or chemotherapeutic agents, and that Townsend et al. teach that increased Mcl-1 expression due to chemotherapeutic agents is mediated by ERK activation. It is alleged, however, that such increased Mcl-1 expression is associated with only transient protection against apoptotic stimuli, and that the specification does not teach how to affect changes in Mcl-1 protein levels for a sufficient duration to treat a disease by utilization of the claimed Mcl-1 gene regulatory element. It is further stated that the specification provides no guidance for using an Mcl-1 gene regulatory element of the invention to modulate Mcl-1 polypeptide expression and, therefor, induce apoptosis, for example, in

cancer cells, or prevent apoptosis, for example, in neurons. As discussed above, the claims are directed to compositions, and the specification discloses specific, substantial and credible utilities for the claimed Mcl-1 gene regulatory element. As such, it is submitted that such issues are not particularly relevant to the patentability of the pending claims.

In summary, the claimed Mcl-1 gene regulatory elements are compositions of matter, and the specification discloses specific, substantial and credible utilities for the claimed regulatory elements. Accordingly, it is respectfully requested that the rejection of the claims as lacking utility be removed.

C. Rejection under 35 U.S.C. § 112

The objection to the specification and corresponding rejection of claims 1 to 21 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement respectfully traversed.

The claims are rejected essentially for the reasons set forth respect to the alleged lack of utility. However, for the reasons set forth above, it is submitted that the claimed Mcl-1 gene regulatory elements have a patentable utility and, therefore, that the specification clearly teaches one skilled in the art how to make and use the regulatory elements of the invention without undue experimentation. Accordingly, it is respectfully requested that the objection to the specification be withdrawn and that the corresponding rejection of the claims as allegedly lacking enablement be removed.

D. Regarding Claims 10 to 21

Although the Office Action generally states that claims 1 to 21 are rejected as lacking utility and enablement, no specific rejections have been made with respect to the subject matter of claim 10 to 21. Instead, all of the rejections are directed only to the claimed Mcl-1 gene regulatory element, which is the subject matter of claims 1 to 9.

Claims 10 to 19 are directed to nucleic acid molecules encoding an Mcl-1 polypeptide, and to compositions containing such nucleic acid molecules. Claims 20 and 21 are directed to oligonucleotides that can specifically hybridize to nucleotide sequences of a nucleic acid

molecule encoding an Mcl-1 polypeptide. As stated above, no specific arguments have been set forth in the Office Action as a basis for rejection the subject matter of claims 10 to 21. Accordingly, it is respectfully requested that the Examiner issue a notice that at least claims 10 to 21 are allowable.

In view of the amendments and the above remarks, it is submitted that all of the claims are in condition for allowance and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

Date: October 2, 2001

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